Issues in Immunization in Developing Countries

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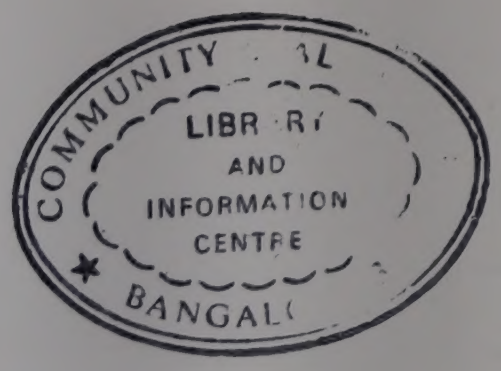

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ISSUES IN IMMUNIZATION IN DEVELOPING COUNTRIES

An overview

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1. INTRODUCTION

It has been estimated that of every 1000 children born in developing countries, "5 will grow up crippled by poliomyelitis, 10 die of neonatal tetanus, 20 die of whooping cough (pertussis) and 30 or more die of measles or its complications." (Editorial, 1985a). The World Health Organization (WHO) has calculated that during 1984, measles, pertussis, tetanus, poliomyelitis, diphtheria and tuberculosis were together responsible for the death of about 4 million children in developing countries and caused an additional 4 million children to become physically or mentally handicapped (Henderson, personal communication). The reason why the mortality and morbidity associated with these six diseases is of particular concern is that for more than twenty years they have been preventable by immunization. Vaccines are available which are safe, relatively cheap, easy to administer and which are generally effective, providing long-lasting protection with few serious side-effects (Dick, G.,1985).

In a number of countries such as Europe and North America, the use of these vaccines has played an important role in greatly decreasing the incidence of these diseases to the point where, with a few exceptions, they no longer constitute problems of major public health importance. In many of these countries the vaccine-preventable diseases have been virtually eliminated, despite the fact that in the 1950s they were often major causes of disability and death (Schonberger et al, 1984). In most developing countries, however, these diseases continue to place a heavy burden on families and communities and on their health services. Although there have also been some important advances in the control of vaccine preventable diseases in developing countries (Foster et al, 1984; Risi, 1984), for the most part they remain priority causes of morbidity and mortality, particularly among children.

Why are these diseases still such major problems in many developing countries and what lessons can be learnt from our failure to control them despite the availability of well proven technology? What are the obstacles to their prevention and how can these be overcome? What are

the implications for other primary health care (PHC) activities of our inability to transform potential control into reality? This latter question is particularly important since many PHC activities are of less proven value than immunization in the prevention of disease, particularly when they make the leap from small scale interventions to national programmes (Gwatkin et al, 1980; Morley et al, 1983; Vaughan & Walt, 1984).

These are some of the immunization issues which are raised in this publication, although unfortunately it is usually not possible to provide simple universal answers for their solution. In order to restrict the discussion to a manageable size, it will be limited to the six vaccine-preventable diseases already mentioned and to the problems associated with their control in developing countries. There will be no attempt to cover new vaccines which are currently being developed for other priority diseases in developing countries (for example malaria and certain diarrhoeal diseases) nor will there be any discussion of additional vaccines which are sometimes included in routine immunization programmes (for example yellow fever or Japanese B encephalitis). Furthermore, this publication will not include the use of currently available vaccines for specific groups (for example refugees and displaced communities); for outbreaks of preventable diseases (for example meningococcal meningitis and cholera); or for particular clinical problems (for example immunologically compromised individuals or the post-exposure use of tetanus and rabies vaccines).

This publication is aimed at people from a wide range of disciplines who would like an introductory overview of some of the current issues in immunization in developing countries. It is intended to be descriptive rather than prescriptive. Throughout, the term "immunization" is used for the process of administering vaccines. "Vaccination" is only used when a clear differentiation is being made between the administration of a vaccine and the development of immunity.

2. VACCINE-PREVENTABLE DISEASES: diphtheria, pertussis, tetanus, poliomyelitis, measles and tuberculosis

It is obviously somewhat artificial to group together the six vaccine-preventable diseases except in so far as they predominantly affect children, and vaccines are available for their prevention which are generally safe, effective, relatively easy to administer, epidemiologically and economically justifiable for use in national programmes and which provide long-lasting protection - although exactly how long the protection lasts still remains to be seen (Editorial, 1985b; Kjeldsen et al, 1985; Mathias & Schechter, 1985). Tuberculosis is the major exception to both these generalizations since it causes death and disability in adults as well as in children and there is a continuing debate about the efficacy of the available vaccine, BCG (Clemens et al, 1983; Collins, 1984; Curtis et al, 1984; Daniel, 1982; ICMR/WHO, 1980; Lagrange, 1984; Ten Dam et al, 1976).

There are a number of reasons for the different findings of research which has assessed the protection afforded by BCG. These range from possible methodological problems of some of the studies (Clemens et al, 1983) to variations in the epidemiological characteristics of tuberculosis in different communities (Collins, 1984). However, the most serious forms of this disease, tuberculous meningitis and miliary tuberculosis, do most frequently affect children and there is little doubt that their occurrence is decreased by BCG (Ten Dam & Hitze, 1980).

Apart from the two characteristics which these diseases have in common (that they predominantly affect children and that vaccines are available for their prevention), there are a number of ways in which the vaccine-preventable diseases differ. The factors which cause these differences may be grouped into three broad categories, depending on whether they relate to the causative organism (agent factors), to the people affected (host factors), or to the environment in which they live. A knowledge of these different factors is essential to our understanding of how and why vaccine-preventable diseases differ, both

between and within countries, in terms of their incidence and prevalence, seriousness and community concern. It is also important for the identification of appropriate interventions - including immunization programmes. It is because these factors vary from community to community that there can be no universal blueprint for immunization policies.

Agent factors

An obvious difference between these six diseases is that the organisms which cause them are not the same, which has a number of implications for management and control. Measles and poliomyelitis are viral diseases whilst tetanus, diphtheria, pertussis and tuberculosis are caused by bacteria. For the latter two diseases it is the bacteria themselves which give rise to the pathological changes, whilst in the case of both diphtheria and tetanus it is the toxins produced by the bacteria which are primarily responsible for the pathogenicity of these diseases.

There are also differences in the ways in which the organisms which cause the vaccine preventable diseases are spread. Tetanus enters the body through broken skin, poliomyelitis is predominantly transmitted by the faeco-oral route (in developing countries) and measles, pertussis, diphtheria and tuberculosis are primarily spread by droplet infection. The conditions which these organisms require to exist outside the body also differ. For example, tetanus is able to remain viable for many years in the form of spores whilst measles is effectively unable to survive outside the body, requiring direct person-to-person transmission.

Most unimmunized children in developing countries will be infected by the organisms which cause measles, pertussis, poliomyelitis and tuberculosis although many more children will die from measles than from the other three diseases. On the other hand, whilst a relatively small number of children will contract tetanus, a high percentage of those who are infected will die. Each of these diseases therefore has different incidence, disability and case fatality rates.

Host factors

Another important way in which these diseases differ is the groups who are affected. The most obvious characteristic is age. For example, tetanus is a major cause of neonatal mortality - as many as 70% of deaths during the first month after birth are caused by this disease in some rural communities (Stanfield & Galazka, 1984); pertussis has its major impact on childhood mortality during the first year of life (Muller & Leeuwenburg, 1985; Voorhoeve et al, 1978); and measles is one of the most important causes of disease and death between the ages of six months and five years (Assaad, 1983; Walsh, 1983).

In addition to age, the nutritional status of children has a major influence on diseases such as measles and tuberculosis. Whilst nutrition does not affect the number of children who will contract measles in the absence of immunization, it has a profound impact on the severity of this disease. Children who are malnourished are much more likely to die from measles than those who are well nourished. Not only is the severity of certain vaccine-preventable diseases increased by malnutrition, but the vaccine-preventable diseases themselves, in common with other childhood infections, have an adverse effect on the nutritional status of children. Their control is therefore likely to have an impact on health which is much more extensive than simply decreasing the morbidity and mortality which is directly associated with these six diseases (Henderson R, 1983; Feachem & Koblinsky, 1983).

Environmental factors

The disability and mortality associated with these diseases may also be affected by a number of more general factors. These include overcrowding, which facilitates transmission; the provision of health care, which can decrease the occurrence of complications; and sanitation, which may affect the spread of polioviruses (although it is more likely to be one of the factors which determines *when* rather than *if* children are infected with these viruses, since prior to

immunization, poliomyelitis was a common disease in many countries with relatively sophisticated sanitation facilities). Culture and education may also affect the incidence and severity of these diseases. They have a bearing on practices which may cause some of the diseases, for example the application of certain traditional poultices to the umbilical cord following delivery is one of the major causes of neonatal tetanus. They may also increase the occurrence of complications, for example customs of confining or withholding food from children with measles.

3. THE VACCINES

In the same way that the vaccine-preventable diseases differ, so too do the vaccines. These differences have a number of implications for the storage requirements of the vaccines, their methods of administration (whether, like live virus polio vaccine, they can be taken by mouth or if they must be given by injection) and their production costs. Furthermore, there are differences in the types of immune response which they elicit, their side-effects, contra-indications to their use, their effectiveness, the number of doses which must be given, the minimum age for administering the first dose and the interval between doses (see Table I).

These differences raise several issues which are fundamental to planning immunization programmes. First, there are some requirements for the storage and administration of the vaccines which should be guaranteed before embarking upon any action. If sufficient training, supervision and resources are not available to ensure that the vaccines are correctly stored and administered, then they may be spoilt. If this happens they will not stimulate antibody production so effectively and protection may be reduced to low levels, even to zero. This is likely to have a number of serious repercussions on the attitudes of the community to immunization in general and is certainly a waste of scarce resources such as time and money.

Secondly, it needs to be appreciated that contra-indications to immunization are rarely absolute. They depend on the severity of the disease in the specific community under consideration, and on the frequency of contact between the people and the health services. Similarly, the importance of possible side-effects of the vaccines must be considered in relation to the likelihood of children developing serious complications following natural infection.

Table I

Characteristics of vaccines included in the Expanded Programme on Immunization. (Adapted from Henderson, R. [1984]c).

Vaccine	No. of doses	Timing of doses	Route of admin.	Stability at 37 C
Measles	1	From 9 months where measles remains a problem for infants: from 12-15 months elsewhere	Deep subcutaneous or intramuscular injection	Previously about one wk Approx. one month with recently developed vaccines
BCG	1	From birth	Intradermal injection	Approx. one week
DPT	3	From 6 weeks of age, at interals of 4 wks. Two doses may suffice if a high potency vaccine is given at 4-6 month intervals. An additional dose is frequently given during the 2nd year of life	Intramuscular injection	Approx. one week
Oral Polio	3	From birth, but more usually from 6 wks of age, at intervals of 4 wks. An additional dose frequently given during 2nd year of life The impact of immunization at birth needs further evaluation	Oral	Approx. one day
Inactivated Polio	2	From 3 months of age, at intervals of 4-6 mos. The effects of a single dose, an earlier starting age & shorter intervals between doses being evaluated	Deep subcutaneous or intramuscular injection. May be combined with DPT	Approx. one week
Tetanus Toxoid	2	For use in prevention of neonatal tetanus, first dose at first contact with susceptible woman, 2nd dose 4 wks later. In previously immunized women, 1 additional dose during pregnancy sufficient	Intramuscular injection	Approx. two months

Finally, recommendations for the age when vaccines should first be given and how long the period should be between doses are usually based on optimal antibody responses determined under research conditions. However, there is often a degree of flexibility around these recommendations (EPI, 1979b; Galazka, 1983) when the immune responses will be protective, if not ideal. Depending on the severity of the diseases, the age groups predominantly affected and the development of the health services, a balance will need to be achieved between what is ideal and what is possible (accepting, of course, that there are limits to the flexibility of immunization schedules, and that outside these limits they will not provide protection and their use cannot therefore be justified).

Of the six vaccines, BCG and pertussis are the least satisfactory in terms of efficacy and, in the case of pertussis, side-effects. Although both vaccines are being further refined, the research which is needed is much more advanced for pertussis (Manclark & Cowell, 1984), possibly because tuberculosis, unlike pertussis, is no longer a major problem for the industrialized countries where most of the research is funded and carried out (EPI, 1985). The problem of vaccine research is well exemplified by the fact that in the same year that the National Institute of Allergy and Infectious Diseases (USA) spent nearly US$ 4 million on research on genital herpes it spent just a little over US$ 1 million on poliovirus research (Jordan, 1984). There are obviously a number of reasons for this disparity, but differing priorities between developed and developing countries for vaccine research must be an important factor. Fortunately, much of the research which is needed is of an applied rather than a technological nature and, as such, will frequently be carried out most effectively in developing countries as part of the process of planning, implementing, monitoring and evaluating immunization programmes (EPI, 1984a).

Technological advances continue to improve the vaccines and such developments will facilitate their provision and overcome some of the obstacles to effective coverage. For example, the costs of producing

inactivated polio vaccines have recently fallen significantly and research is underway to decrease the number of doses which are needed from three to two and even, possibly, to a single dose (Salk, 1984; Swartz et al, 1984; Van Wezel et al, 1984). Developments are also taking place with measles vaccine, which have already greatly reduced its sensitivity to temperature by making it less thermo-labile, and which may possibly decrease the minimum age at which it can effectively be given. New ways of administering the vaccine, by aerosol rather than by injection are also being explored (Sabin, 1983).

Whilst in general there is little controversy about the basic forms of the vaccines, there is an on-going debate about which polio vaccine is most appropriate for use in developing countries. The main differences and some of the corresponding advantages and disadvantages between the live and inactivated forms of this vaccine are summarized in Table II.

Table II

Selected differences between live and killed polio vaccines which have implications for their use in national campaigns*

Characteristic	Oral Polio Vaccine	Killed Polio Vaccine
Proven to be effective in national control:		
- developed countries	Yes	Yes
- developing countries	Yes	No (so far has not had an opportunity to demonstrate this)
Type of immunity	Humoral & intestinal immunity (although the significance of the latter for CNS invasion is unsure); produces antibody rapidly & blocks alimentary spread, therefore very good for the control of epidemics	Humoral immunity (although possibly also undetectable amounts of secretory antibodies)
Seroconversion	Some evidence of suboptimal seroconversion in developing countries - although seronegative children may be "primed"	Seroconversion good
Protection provided by vaccine	Probably life-long - may also induce immunity in contacts	Probably life-long - may require boosting
Earliest age for vaccination	Possibly at birth because secretory antibodies are not affected by maternal antibodies	Over 6 weeks because of interference by maternal antibodies
Number of doses of vaccine required	Three (at least)	Usually three; two may be adequate (possibly one)
Side-effects	Generally few - can rarely mutate & revert to neurovirulence causing paralysis in recipients or contacts	Few - potential problems of vaccine not completely inactivated
Cost of vaccine	Low	Higher (although coming down fast)
Availability	Adequate	Inadequate currently
Storage	Vaccine heat sensitive therefore effective cold chain essential	Cold chain less important (although still needed)
Administration	Simple (oral drops)	Requires needle and syringe (however may be given as a combined vaccine with DPT - although schedules may adversley affect the pertussis component)
Coverage needed for control	May decrease poliomyelitis disproportionately to the coverage because of circulating vaccine virus; a single dose provides full immunity in a percentage of recipients thereforer a small number of drop-outs will be protected	May affect the circulation of wild virus in the community but coverage needs to be high

* This is an extremely complex and controversial issue - see references for further details.

References

Boffey, 1977; Editorial, 1977; Editorial, 1978; Editorial, 1983; Editorial, 1984b; EPI, 1981; EPI, 1983b; Ghosh, 1984; Hinman, 1984; Horstmann, 1982; John, 1985; John & Jay et al, 1972; Krishnan et al, 1983; Martin, 1984; Melnick, 1978; Robsinson, 1982; Sabin, 1984; Sabin, 1985; Salk & Salk, 1984; Stoeckel et al, 1984; Swartz et al, 1984; Vallancourt, 1984; Van Wezel et al, 1984.

4. EPIDEMIOLOGICAL APPROACHES TO IMMUNIZATION

This brief overview of some of the differences between the vaccine-preventable diseases is based on information obtained from epidemiological studies. One of the major contributions which epidemiology has made to our understanding of these diseases is that there are a number of interacting factors which give rise to their differential distribution.

General principles

From epidemiological surveys we can obtain important information about the vaccine-preventable diseases. First, are the individual diseases serious health problems - where do they come in the hierarchy of priorities? For example, it is only relatively recently, with the development and implementation of lameness surveys, that the extent of the residual paralysis caused by poliomyelitis is being fully appreciated in many developing countries (Ofosu-Amaah, 1984). Measles, pertussis, tetanus and tuberculosis are all well documented as being major health problems in most developing countries, with a high ranking position in the list of priorities (Walsh & Warren, 1979; Berggren et al, 1981; Ghana Health Assessment Project Team, 1981).

In contrast, relatively little is known about the distribution of diphtheria in developing countries. There is some evidence that certain communities may be protected from the more serious forms of this disease by the development of antibodies in response to minor skin infections with the causative organism. These then confer immunity to the more serious forms of this disease. The implication of this is that diphtheria may become more of a public health priority in developing countries as hygiene conditions improve, a problem which, for different reasons, may also apply to epidemics of poliomyelitis (Khuri-Bulos et al, 1984). However, even though diphtheria may not currently be a priority disease, because the vaccines for tetanus, pertussis and diphtheria are, for purposes of the routine immunization

of infants, combined as a single vaccine, its inclusion in the basic immunization schedule adds very little to the costs or organizational problems of immunization programmes.

Apart from describing the extent of the problem (and therefore helping planners to decide what proportion of the available resources should be directed towards these diseases rather than to any of the other pressing health problems), epidemiological studies can also identify the characteristics of the people who are most seriously affected, both in terms of morbidity and mortality. This information is essential if we are to be able to target specific groups and to ensure that the vaccines are given early enough to prevent the majority of cases and, at the same time, are not wasted on children who are already immune as a consequence of natural infection.

The analysis of data from routinely collected statistics and ad hoc surveys needs to be used in combination with the findings of serological studies which can determine when the response to the vaccines is optimal, thus providing an indication of the minimum age for effective vaccination. These data enable us to define the period between susceptibility to a certain disease and responsiveness to the appropriate vaccine. For measles this is of relatively short duration, which has created difficulties for immunization programmes (Griffith, 1975). Serological studies also provide information about the optimal periods between immunizations and the duration of protection.

For example, tetanus is a major problem during the neonatal period. Whilst the routine immunization of infants is an investment for the future, to protect newborn children necessitates the immunization of women, either prior to or during pregnancy, so that they can transfer (passive) immunity to their children. Similarly, before providing measles vaccine, it is important to know the age at which most children will already be immune as a result of natural infection (Chin & Thaung, 1985), and to appreciate that many children younger than nine months old will not have an adequate response to the vaccine because of the antibodies which are passively transferred from the mother across the placenta. Such information enables planners to

identify an upper and lower age limit for children to be included in immunization programmes.

In addition to enabling health planners target the specific age group which needs to be immunized, epidemiological studies have also identified particularly high-risk groups in terms of person, time and place. For example, in South Africa measles affects black children much more seriously than white children (Dick, 1975). In Israel, poliomyelitis has a considerably higher incidence among non-Jews than among Jews (Goldblum & Swartz, 1984). Such information enables us not only to identify high-risk groups who warrant particular attention but also leads us to ask why this should be in terms of causative factors and the provision and utilization of services. It is ironic, if not altogether surprising, that it is often the groups at greatest risk from these diseases who are also least likely to have access to appropriate health services.

The provision of health care is an important "environmental" factor in the distribution of vaccine-preventable diseases - the vaccines themselves may alter the epidemiological characteristics of the diseases. For example, incomplete coverage may give rise to increasing numbers of older people who are unprotected either by vaccination or following natural infection. Similarly, as increasing numbers of women of child bearing age acquire their immunity to measles from immunization rather than from natural infection, as the coverage rates for ante-natal tetanus immunization increase and with the advent of more potent pertussis vaccines, the effects of these developments on passively transferred maternal immunity will need to be monitored - since this will affect the response of infants to vaccines given during their first few months of life.

Epidemiological and serological surveys are also important for the surveillance and evaluation of immunization programmes which have been implemented. These will be covered in more detail in a later section.

Epidemiological concepts

There are a number of epidemiological concepts which are frequently encountered in the literature and in discussions about immunization programmes. These are sometimes not clearly defined and as they have an important bearing on approaches to immunization policy they require clarification.

i. Protection. There are at least three different components to any assessment of the protection afforded by a vaccine: potential protection, probable protection and "proven" protection. These different concepts relate to the number of people who are vaccinated (coverage), to the proportion of people who have been vaccinated and who subsequently develop detectable antibodies (seroconversion) and to the proportion of vaccinated individuals who, when they come into contact with the causative organism are actually prevented from developing the disease (efficacy). The differences between these parameters will vary depending upon the disease, the accuracy of routinely collected statistics, the vaccine and the quality of the immunization programme.

An estimation of coverage provides an indication of the combined effects of the provision and utilization of immunization services. It is an assessment of the number of children who have been fully or partially vaccinated during a defined period as a proportion of the total number of children who require immunization in terms of the defined target population of the programme. Information for coverage rates may be obtained from rouinely collected statistics, although since these are often incomplete and inaccurate, such data will usually need to be supplemented by ad hoc surveys (EPI, 1982; Henderson & Sundaresan, 1982). In general, immunization coverage rates in developing countries are poor (Keja & Henderson, 1984), although for some vaccines they have also been far from satisfactory even in developed countries (Stuart Harris, 1979). As recently as 1985 it was necessary to mount a major campaign in the United Kingdom to increase the uptake of pertussis vaccine in the face of an anticipated epidemic.

Recent estimates (EPC, 1985a) indicate that less than 40% of children in developing countries have completed their immunization against polio, diphtheria, pertussis and tetanus, the rates being even less for measles and ante-natal tetanus immunization (Table III). Whilst these coverage rates obviously leave much to be desired, it should be appreciated that major advances have been made since the early 1970s when immunization coverage was much lower; when many countries did not have systems for routinely recording or estimating such statistics; when the quality of the vaccines which were being administered was less adequately controlled or monitored, and when there was generally less emphasis on targeting children under the age of one year.

Seroconversion studies assess the presence or absence of specific immunoglobulins which can be detected in the blood of children and adults following vaccination or natural infection. From serological surveys the proportion of the population who are sero-positive or sero-negative can be determined - that is, the proportion of people who do or do not have protective antibodies to particular infectious diseases. Whilst the presence of detectable immunoglobulins above a predetermined concentration is usually evidence of protection this is not always the case. Conversely, the absence of such immunoglobulins is not always an indication of susceptibility. (There are several reasons why these apparant contradicitions may arise, including the sensitivity of available techniques for measuring circulating antibodies and the fact that there are a number of other protective components of the immune response in addition to specific antibodies, notably cell-mediated immunity). Similarly, following the administration of BCG it is also not always possible to assume that individuals will be protected from tuberculosis merely because they have had a satisfactory "take" following vaccination.

Table III Estimated immunization coverage with BCG, DPT, poliomyelitis, measles, and tetanus vaccines in developing countries ranked by surviving infants, based on data available as of July, 1985.

Country	Newborns surviving to 1 year of age (millions)	Immunization coverage (%)				
		Children less than 1 year of age				Pregnant women
		BCG	DPT III	POLIO III	MEASLES	TETANUS II
India (4)	21.74	65	51	37	...	42
Indonesia (4)	4.59	56	6	7	7	22
Nigeria	4.11	...	...	...	...	...
Pakistan (4s)	3.46	73	64	65	80	24
Bangladesh (4)	2.95	2	2	1	1	1
Brazil (4)	2.83	79	67	99	80	...
Mexico (4)	2.46	24	26	91	30	...
Iran (4s)	2.02	10	68	65	69	4
Vietnam (3)	1.66	5	5	2	4	...
Philippines (3)	1.56	76	61	58	30	...
Egypt (4s)	1.54	53	57	67	41	20
Ethiopia	1.45	16	9	9	16	3
Turkey (3)	1,40	65	56	59	30	...
Zaire (1)	1.29	34	16	18	20	...
Burma (4)	1.29	24	8	1	...	16
South Africa	1.11	...	...	...	...	...
Thailand	1.05	81	57	56	7	31
Kenya	0.98	...	...	...	...	...
Tanzania	0.95	84	9	56	82	35
Rep. of Korea (3)	0.92	84	69	78	...	...
Morocco (3)	0.91	70	48	48	42	...
Colombia (4)	0.86	72	41	60	42	6
Sudan (4)	0.85	7	4	4	3	2
Algeria (1)	0.81	59	33	30	17	...
Argentina (3)	0.70	64	65	64	62	...
25 countries	63.49	49	37	37	19	19
Other developing countries	17.36	43	33	32	28	8
Sub-total developing countries (excluding China)	80.85	48	36	36	21	17
China (45)	19.23	50	63	78	74	...

(1) 1981 coverage data
(2) 1982 coverage data
(3) 1983 coverage data
(4) 1984 coverage data
(s) survey data
... no information available

Source: EPI, 1985a

The efficacy of a vaccine is calculated by comparing the attack rate in unvaccinated individuals with the attack rate in vaccinated people:

Vaccine Efficacy:

$$\frac{\text{Attack rate in unvaccinated - Attack rate in vaccinated}}{\text{Attack rate in unvaccinated}} \times 100$$

This measure of protection takes into consideration the fact that some children who are vaccinated (coverage) will, for a number of reasons, not develop protective immunity. It will also take account of the fact that the serological status of children is not always an indication of whether or not they will contract the disease. What is important about this measure of protection is that it can only be estimated retrospectively for a given immunization programme, because of the diverse factors which may cause children to contract these diseases despite vaccination. Both seroconversion rates and estimates of efficacy require the collection of specific data in addition to those which are routinely recorded by health workers.

ii. Herd immunity. With the exception of tetanus, all of the organisms which cause the vaccine-preventable diseases depend on people for their survival and dissemination. The polio virus is able to survive for several months in sewage and the bacteria which causes tuberculosis can remain viable for several weeks outside the body under exceptionally favourable conditions. However, the agents of measles, pertussis and diphtheria can only exist for very short periods of time outside the environment provided by their human hosts. In general, then, these diseases depend for their continued existence on someone with an infection coming into contact with someone who is susceptible to the infection. As the number of susceptible people decreases in any community, the chances of an infective person coming into contact with a susceptible individual also decrease (hence the characteristic periodicity of measles, with epidemics occurring when the proportion of susceptible people has risen above a certain level). When more than about 90% of the community are protected by either natural infection or immunization the organisms cannot spread and,

apart from isolated cases, will effectively die out. This percentage varies from disease to disease and also depends on whether the total population or only new susceptibles are under discussion. For some of the vaccine-preventable diseases coverage may need to be much higher than 90% (Swartz, 1984).

This concept of the indirect protection of susceptible individuals is known as herd immunity and it has been demonstrated both theoretically, using mathematical models, and in reality. The protective potential of herd immunity depends on the population density and on the amount of mixing, both between and amongst different groups in the community, which affects the opportunities for transmission. It also varies with the infectiousness of the organism and its potential to move from one geographical region to another - easier, for example, in the case of measles than poliomyelitis. In addition, it is affected by the size of the community, since a 90% coverage will clearly leave many more susceptible people in an urban community of one million than it will in a town of 10,000 (Fox et al, 1971; Fox, 1983; Nathanson, 1984; Yorke et al, 1979).

Even more important than the nature and frequency of contact and the absolute numbers, however, is the distribution of the susceptible people within the population. For example, if 10% of the community are unprotected, the possibility of an epidemic occurring is much less if these people are evenly distributed throughout the community than if they mostly constitute a subgroup of the population who have poor provision or utilization of immunization services. This has important implications for setting the objectives of immunization programmes or evaluating them from service activity data (for example, coverage statistics). It is not only the proportion who remain unimmunized but their distribution within the community which is important for the prevention of epidemics (Langmuir, 1971).

Although herd immunity may confer some protection to individuals who have not been immunized and, depending on a number of factors, the impact of immunization programmes may be disproportionate to their coverage (Nathanson, 1982; Roberts, 1984), this should not encourage a

laissez-faire attitude to immunization coverage. The aim should be to immunize everyone.

iii. Eradication and Control.

There are basically two terms which need to be clarified in terms of eradication: global eradication, which implies the world-wide interruption of an infection which, under normal conditions, is irreversible and regional eradication (or elimination), when an infection has been so modified in a country or continent that it ceases to be transmitted in that area. The control of an infectious disease involves the continued limitation of incidence to "acceptable levels" without necessarily implying the total interruption of transmission. An analogy which has been used to differentiate between eradication and control is the situation following a major fire - whether it is "extinguished" or merely "under control" (Stuart Harris, 1984).

One of the great achievements of preventive medicine has been the global eradication of smallpox, nearly 200 years after Jenner first discovered a preventive measure for this disease. If it was possible to eradicate smallpox, why has this not been achieved for the other vaccine-preventable diseases, and what is the likelihood of their eradication being accomplished in the near future?

There are a number of pre-requisites which are essential before a disease could be considered for global eradication. It is important to demonstrate that eradication is technically and economically feasible; that available techniques have the potential to achieve global eradication by their use in accomplishing regional eradication; that sufficient resources are available - technical, financial and human; that an eradication programme will not have a negative effect on other on-going activities; that eradication is a priority for both developing and developed countries and that the implications of not eradicating the disease are serious (Hinman, 1982). Concerning the last two points, it is worth noting that the US$ 32 million invested by the United States of America over 12 years in the smallpox

eradication campaign is now saved by them every 3 months because it has been possible to stop routine vaccination and the maintenance of quarantine barriers (Hopkins et al, 1982).

There are also a number of epidemiological considerations (Nathanson, 1984). These primarily relate to the parameters which determine perpetuation, such as transmissibility (the proportion of susceptible contacts infected per existing case) and a number of population variables including size, turnover and the percentage of people who are immune (Fox et al, 1971; Fox, 1983). An understanding of these factors is important for both eradication and control programmes, for example by enabling available resources to be concentrated on high risk groups or by exploiting seasonal troughs (Yorke et al, 1979).

Of the vaccine-preventable diseases, only measles and poliomyelitis would appear to meet the pre-requisites for global eradication. However, despite the optimism and enthusiasm for eradication which exists, (Gregg, 1984; Foege, 1984) for a number of technical, financial, infrastructural, managerial and even political reasons it seems unlikely that this will occur in the immediate future (Henderson, D, 1983). In fact, a major dilemma still exists as to whether movement towards the goal of global eradication of these diseases is even desirable at the present time. Nonetheless, the regional eradication of some diseases may be a realistic objective, for example the recently stated goal to eliminate poliomyelitis from the Americas by 1990. Table IV provides a number of characteristics of measles and poliomyelitis which differentiate them epidemiologically from smallpox and which would make their eradication more difficult.

One of the most important aspects of the eradication of smallpox was that high vaccine coverage was not essential. "Surveillance and containment" approaches achieved eradication with rates as low as 50% in some communities. For both measles and polio, depending on the target groups of the immunization programme, it would be necessary to achieve near universal coverage, particularly if the young and the few older susceptibles were to be indirectly protected by herd immunity.

Table IV

Factors affecting the eradication potential of measles and poliomyelitis compared with smallpox

(Chin, 1984; Fenner, 1982; Foege, 1984; Hinman, 1982; Hopkins et al, 1982; Miller & Foege, 1969; Stuart-Harris, 1984)

Characteristics of diseases and vaccines	Smallpox	Measles	Poliomyelitis **
Priority disease:	Yes	Yes	Yes
International implications	Serious	Only for countries with national eradication	Only for countries with national eradication
International concern	High	Poor	Moderate
Subclinical cases	None	A few	Many
Clinical diagnosis	Unique & easily recognizable rash	Rash may be confused with that of other diseases	Difficult because of high rate of inapparent infection or mild illness with non-specific signs
Detection of infectious cases	Easily identified - characteristic rash	Infectious prior to development of characteristic rash	Infectious prior to the development of classical symptoms, ie. paralysis
Degree of infectivity	1/3 household of contacts will be infected - spreads relatively slowly	3/4 susceptible household contacts will be infected - rapid spread with explosive outbreaks	Highly infectious to susceptible contacts - spreads rapidly & may cause epidemics
Animal reservoir or vector	Nil	Nil	Nil
Chronic carrier state	No	No	No - although virus may be excreted for several weeks it is only infective for a relatively short period.
Immunity following: - infection - vaccination	 Life-long Long-term	 Life-long Long-term	 Life-long Long-term
Serotypes	One	One	Three
Seasonality	Yes	Yes	Variable: may occur throughout the year
Mode of transmission	Close person-to-person contact	Droplet spread	Usually direct via faeco-oral route
Average age of infection	4-5 years	12-18 months	12-24 months
Age at which vaccine safe and effective	Birth	9 months	6 weeks, probably at birth.
Dose of vaccine required	One	One	Multiple
Recognition of immune individuals	Easy - vaccination scar & pock mark	Difficult except by serological survey	Difficult except by serological survey
Surveillance	No records required because of scar	Records required	Records required.
Cost of vaccine	Cheap	Expensive	Cheap (killed vaccine more expensive)
Administration of vaccine	Easy - bifurcated needle	Difficult - needle & syringe	Easy - oral drops for live virus vaccine; Difficult - needle & syringe for killed vaccine
Cold chain requirements	Minimal	Moderate	Maximum (for live virus vaccine)
Vaccination coverage required for eradication	50% or less	Universal or near universal coverage	Universal or near universal coverage
Control strategy	Selective ring vaccination	Improved nutrition etc plus vaccination	Improved sanitation plus vaccination
	Intermittent or itinerant campaigns possible	PHC structure capable of delivering routine vaccines	PHC structure capable of delivering routine vaccines: also mass campaigns

** With live polio vaccine there remains the likelihood of a very small number of cases of vaccine associated paralytic poliomyelitis.

Since it is likely that to achieve rates as high as this will take many years through routine immunization services, it would be necessary to initiate mass campaigns in order to eradicate these diseases. For this reason alone it seems likely that control rather than eradication is a more feasible policy for most governments, although the elimination of polio has already been or, at least is well on the way to being successfully accomplished in some developing countries using mass campaigns, for example Cuba and Brazil (Risi, 1984; Cruz, 1984).

Although it is conceivable that international political instability and socio-cultural factors may have compounded the problems of access encountered during the smallpox eradication campaign (Henderson, 1982), of much greater importance for goals of global eradication are the changes in health policy which have occurred since the days of this campaign. The last case of "natural" smallpox was diagnosed in October 1977. The Alma Ata conference on Primary Health Care which took place the following year, orientated health care away from disease-specific interventions towards a broad-based development strategy. Of course, within this overall approach there are interventions directed towards specific diseases - immunization itself is an obvious example. However, the main thrust of the reorientation is the emphasis which is currently placed on the use of available resources to build up an appropriate and equitable health care infrastructure, involving the community and sectors other than health which have an impact on people's well being (Walt & Vaughan, 1981). To mount major mass eradication campaigns would be flying in the face of the philosophy of PHC, and it is doubtful whether the use of scarce resources could be justified in eradicating these diseases globally, before the goals of the PHC initiatives currently under way have been achieved.

However, this is not to suggest that immunization initiatives do not have great potential to strengthen the basic health care infrastructure. PHC services have been extremely difficult to implement in many countries and it is clear that the vaccine-

preventable diseases will not be controlled merely by adding immunization to a rhetoric that does not materialize. In many regions institutional and managerial capacity are important constraints to realizing the goals of primary health care (Vaughan & Walt, 1984). It is possible that this capacity will be greatly improved by involvement with implementing limited programmes with clearly defined and relatively rapidly attained and measurable objectives. Immunization is such a programme which embraces a wide range of activities including training, management, delivery and surveillance systems. Immunization programmes should therefore provide opportunities to strengthen the infrastructural foundations on which other PHC activities could be built (Gregg, 1984; Henderson, D. 1984). Certainly immunization should be included in any "selective" approach to PHC (Walsh & Warren, 1979; UNICEF, 1985).

While the debate between eradication and control continues, it is important for governments to be quite clear about the organizational and technical implications of selecting either of these as national objectives (Nathanson, 1982). At their most simplistic, the options are for control which will be achieved slowly through the expansion of PHC services or eradication which will require the adoption of quite different strategies, for example mass immunization programmes, in order to achieve the high coverage rates necessary. However, it is clearly not an all-or-nothing choice: it is possible for the two approaches to co-exist, for example, by relying on the PHC infrastructure to provide vaccines routinely and to boost this with National days devoted to immunization (National Coordinating Committee, 1984).

5. PREVENTING THE VACCINE-PREVENTABLE DISEASES

There is extensive evidence available to indicate that the vaccine-preventable diseases are major causes of mortality and morbidity in developing countries, and that available vaccines have the potential to prevent these diseases. However, as it is also clear that the achievement of the high vaccine coverage rates necessary to control these diseases is still likely to take a number of years in most developing countries, it is important to place the role of immunization in the overall context of approaches to the prevention of the disabilities and deaths associated with these diseases.

There are three basic principles in the control of infectious diseases; to decrease the pool of infection by reducing the distribution of the causative organism in the environment or community; to interrupt the mode of transmission by preventing the organisms from spreading to susceptible individuals; and to increase host resistance by improving peoples' ability to cope with the organisms should they be exposed to them. Whilst immunization may play a role in all three of these aspects of control, there are a number of other activities which are also important. These will differ depending on the epidemiological characteristics of the disease.

The example of measles

There are no known animal reservoirs of measles and so the pool of infection of this disease consists of people currently suffering from measles. Most children with measles are only infectious for a relatively short period of time, and since there is no effective specific anti-viral treatment for the organism which causes measles (although treatment has an important role to play in the management of many of the complications of this disease) there is no intervention which will affect the pool of infection apart from immunization. Of course, following an epidemic of measles the pool of infection is also decreased.

Similarly, apart from isolating children with measles (which is carried out in some cultures - to the benefit of the community if not of the sick child) or decreasing the opportunities for susceptible children to come into contact with cases of active measles (which may be a problem if there is overcrowding or when young children are taken to markets or other places where large numbers of people congregate) there is relatively little that can be done to decrease transmission. Neither of these options is feasible or even necessarily desirable in most communities, and, in any event, children with measles are most infectious during the relatively asymptomatic prodromal period which occurs before the onset of the characteristic rash of this disease.

Natural infection confers durable life-long immunity and there is no evidence to indicate that this is not also endowed by available measles vaccines. Immunization is therefore clearly one important method of increasing the host resistance to this disease - in fact it is the only means of ensuring that children do not actually develop measles. However, there are a number of other interventions which may decrease the associated disabilities and death.

For example, like many other diseases, measles mortality greatly decreased in the United Kingdom prior to the availability of an appropriate vaccine. This was a consequence of improved social and economic conditions and the effects which these improvements had on family size and overcrowding and on nutrition. With the advent of antibiotics and cheap and effective methods of preventing dehydration, many of the major problems associated with measles (such as the ophthalmic, respiratory and gastro-intestinal complications) should be avoidable by expanding basic diagnostic and curative services (Editorial,1984a; Drew & Bauhaun, 1982). The general development and expansion of health services should also help to decrease the incidence and severity of other diseases which affect the nutritional status of children, and which subsequently increase the risk of measles causing disability or death. It is for this reason that the Expanded Programme on Immunization (EPI) has included such topics as oral rehydration and malaria prophylaxis in its training programmes.

The important lesson from all of this is that although immunization will be the most important intervention for decreasing the incidence of measles, whilst ways of achieving the very high immunization coverage necessary to effectively control or even eliminate it are developed, many other approaches could and certainly should play a part in decreasing the complications and high fatality rates associated with this disease.

The example of tetanus

Tetanus provides another example of the need to attack the vaccine-preventable diseases on a number of fronts. Since the organism which causes this disease is ubiquitous in the soil and in the alimentary tracts of certain domestic animals, there is really very little that can be done to decrease the pool of infection. However, the most important form of this disease encountered in developing countries is neonatal tetanus. This occurs because the organism is transmitted by unhygienic methods of cutting the umbilical cord or as a result of the application to the umbilical stump of traditional poultices which are contaminated with tetanus spores. There are a number of ways in which this transmission may be interrupted: by ensuring that children are delivered by trained health workers, by supporting traditional birth attendants and providing them with sterile dressing packs and by health education. Such activities can, additionally, have an impact not only on tetanus but also on a number of other causes of perinatal and neonatal morbidity and mortality (Rahman, 1982; Rahman et al, 1982; Berggren & Berggren, 1971).

The only method of increasing host resistance to this disease is by immunization. Since children need to have protection to this disease at the time of birth, the vaccine must be given to women during pregnancy, or before. Immunity is then passively transferred from mother to child. The increased provision and utilization of health services will also help, albeit in a small way, to decrease tetanus associated disabilities and death (although it should be emphasized that, unlike measles, the resources required for treating tetanus are much more sophisticated and expensive). However, the control of this

disease is so dependent on immunization that neonatal tetanus mortality rates are a good proxy measure of vaccine coverage.

The example of tuberculosis

In the case of tuberculosis, BCG is the main approach to increasing host resistance (although, as has already been mentioned, there is still controversy about the efficacy of this vaccine in different situations). Improved nutrition, decreased overcrowding and raised socio-economic conditions will also play important roles in helping people to combat this disease - indeed, in the industrialized world these were important factors which contributed to the marked decline in tuberculosis.

However, the main approach to decreasing the pool of infection and interrupting transmission is through early diagnosis and the prompt, adequate treatment of individuals with "open" tuberculosis (that is, tuberculosis in a form which is infectious to other people). Screening programmes, case finding techniques, and the ability to ensure the constant availability of drugs and compliance with treatment regimes which last in excess of six months will all depend on the expansion of health services in developing countries. Such expansion will also play an essential role in the management of the acute complications of pertussis and diphtheria and in the long-term rehabilitation of children crippled by poliomyelitis. Developments in health related sectors such as housing, sanitation and agriculture will also be important.

The Expanded Programme on Immunization

The Expanded Programme on Immunization (EPI) was conceived and initiated during the 1970s in the wake of the justified optimism generated by the impressive achievements of the smallpox eradication campaign. Since its inception it has been very much a collaborative programme, involving WHO, UNICEF, national governments, non-governmental organizations and experts in the field of immunization. The aims of EPI have been to stimulate and support the expansion of

national immunization services and other activities related to the control of vaccine-preventable diseases. The ultimate goal of EPI is to make immunization services available to all children in the world by the year 1990 (EPI, 1984k). The five point action plan of EPI is reproduced in Table V.

EPI has set about accomplishing its goal through a variety of activities. These include advocacy and ensuring that immunization remains "on the agenda"; the collation and distribution of information about the vaccine-preventable diseases (EPI, 1985c) and about recent advances in immunization (EPI, 1984j); the development and implementation of training programmes for a wide range of health staff, from senior managers to village health workers; improving and encouraging quantitative approaches to planning, surveillance and evaluation through assistance with a large number of in-country surveys to assess immunization coverage and estimate the incidence of vaccine preventable diseases; and by the completion of nearly 90 national programme reviews between 1978 and 1984 (EPI, 1985). These evaluations have helped to pinpoint problems with national immunization programmes and to identify obstacles preventing more complete coverage in the specific and differing conditions of Member States. At the same time they have enabled other countries to benefit from both the good and the bad experiences of the countries which have been reviewed.

Whilst the five-point action programme will continue to provide an indication of the priorities for development, the EPI has recently identified a number of areas where immediate actions are required (EPI, 1985a): to provide immunization or information about immunization at every health contact; to reduce drop-out rates between first and last immunizations; to increase the priority being accorded to the control of measles, poliomyelitis and neonatal tetanus; to improve immunization services to the disadvantaged in urban areas; and where required, to accelerate the EPI using approaches similar to national immunization days, assuring that these

Table V

THE EXPANDED PROGRAMME ON IMMUNIZATION

FIVE-POINT ACTION PROGRAMME

(1) Promote EPI within the context of primary health care:

- develop mechanisms to enable the community to participate as an active partner in programme planning, implementation and evaluation, providing the technical and logistical resources to support these functions; and

- deliver immunization services with other health services, particularly those directed towards mothers and children, so that they are mutually supportive.

(2) Invest adequate human resources in EPI: Lack of these resources in general and lack of management skills in particular represent the programme's most severe constraints. Capable senior and middle-level managers must be deisgnated and given authority and responsibility to carry out their tasks. They require training, not only to be effective with respect to EPI, but also to contribute to the understanding and strengthening of the primary health care approach. Reasons for low motivation and performance in the areas of field supervision and management need to be identified in order that appropriate measures can be taken to encourage managers to visit, train, motivate and monitor the performance of those for whom they are responsible.

(3) Invest adequate financial resources in EPI: For the programme to expand to reach its targets, current levels of investment in EPI, estimated now at US$ 72 million per year, must be doubled by 1983 and doubled again by 1990 when a total of some US$ 3000 million (at 1980 value) will be required annually. Over two-thirds of these amounts must come from within the developing countries themselves, the remaining one-third from the international community.

(4) Ensure that programmes are continuously evaluated and adapted as to achieve high immunization coverage and maximum reduction in target-disease deaths and cases: Such adaptation depends on the development of adequate information and evaluation systems. By the end of 1985 at the latest, each country should be able to:

- estimate reliably immunization coverage of children by the age of 12 months with vaccines included in the national programme;

- obtain timely and representative reports on the incidence of EPI target diseases included within the national programme; and

- obtain information on the quality of vaccine so that it is known that the vaccines employed for EPI meet WHO requirments and are potent at the time of use.

In addition, countries should promote the use of periodic programme reviews by multidisciplinary teams comprised of national and outside staff to ensure that operational problems are identified and that a wide range of experience is reflected in the recommendations which are made.

(5) Pursue research efforts as part of programme operations: The objectives should be to improve the effectiveness of immunization services while reducing their costs and to ensure the adequate supply and quality of vaccines. Specific concerns include the development of approaches for delivering services which engage the full support of the community, the improvement of methods and materials relating to sterilization and the cold chain, the acquisition of additional knowledge concerning the epidemiology of the target diseases, further development of appropriate management information systems, and further improvement in the production and quality control of vaccines which are safe, effective and stable.

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strengthen the health infrastructure and contribute to a sustained improvement in coverage. In addition, ongoing actions which need to be pursued further include: strengthening disease surveillance and outbreak control; reinforcing training and supervision; and pursuing applied research and development.

Although essentially a "vertical" programme, EPI is committed to controlling the vaccine preventable diseases within the overall context of primary health care (PHC). Provided that this does not create an imbalance at a national, and particularly at a district level, there should not necessarily be a conflict between promoting PHC as an approach to health service provision and strengthening and improving the quality of this specific PHC activity.

6. PROBLEMS RELATED TO IMMUNIZATION PROGRAMMES

Why are the vaccine-preventable diseases still such a major cause of morbidity and mortality in developing countries despite the availability of effective vaccines and the impressive decline in these diseases in many industrialized, high income countries? First, many developing countries still have very low socio-economic standards of living for the majority of their populations, and it is widely recognized that without improvements in nutrition, water supplies, sanitation, housing, education and other related sectors, improvements in health are slow.

Second, the immunization coverage which has been achieved in developing countries has generally been much lower than the rates in countries where these diseases have been effectively controlled. Furthermore, for a number of reasons which will be discussed later, the vaccines have sometimes not proved to be so effective in developing countries. As with many other aspects of health care, it has not always been possible to obtain similar results simply by moving technology from one setting to another.

In general, immunization coverage in excess of 90% will be necessary for effective control of the vaccine-preventable diseases. The major exception to this may be poliomyelitis, since if the live virus vaccine is used, it is possible that the vaccine virus which is excreted may be disseminated in the community under conditions of poor hygiene and inadequate sanitation (Foster et al, 1984) - although the dissemination of the vaccine virus may not extend much beyond family contacts, in which case the required coverage would not be markedly decreased. However, some susceptible children may become infected by the vaccine virus which could effectively immunize them. It may also be possible to decrease the mortality associated with diseases such as measles if the vaccine is specifically targeted to high risk groups: the poor, the malnourished and people living in overcrowded conditions - although in many developing countries this high risk group will constitute a fairly large proportion of the general population.

However, while such an approach may decrease measles mortality it will not prevent the occurrence of epidemics.

Table III provides information about vaccine coverage as of July, 1985 in different developing countries. It will be noted that very few countries have achieved the high rates necessary for the control of any of the vaccine preventable diseases. The reasons for this are many, but essentially stem from problems related to the appropriateness of the available technology and to a large number of factors related to the provision and utilization of immunization services. A less quantifiable reason is the lack of political will to do what needs to be done, both on the part of politicians and also the medical profession (Ofosu-Amaah, 1984; Robinson, 1984), although this obviously also applies to many other aspects of health care (Heggenhougen, 1984; Segall, 1983).

PROBLEMS WITH THE TRANSFER OF TECHNOLOGY

Immunization schedules

Considering the many agent, host and environmental differences between developed and developing countries, it should come as no surprise that the epidemiological characteristics of the vaccine-preventable diseases differ significantly in these two settings.

Tetanus, for example, has its major impact on adults in developed countries following skin trauma and the contamination of wounds by tetanus spores. In developing countries this disease disproportionately affects quite a different group - children during the first month of life. This difference necessitates the immunization of adult women in developing countries, whilst in developed countries tetanus toxoid only needs to be included in the routine immunization of children (apart from its post exposure use which is similar for both populations).

Similarly, in developed countries measles is a relatively mild disease with its major impact on children during and after their fifth year of

life. In developing countries, however, not only is this a major (sometimes the major) cause of death in children under 5 years of age, but the mean ages for the incidence of the disease and the associated mortality are much younger than in developed countries (Assaad, 1983; Walsh, 1983). Clearly if the high risk children are to be protected against measles it will necessitate the use of measles vaccine in children before the second year of life - which is the age recommended for the administration of this vaccine in the United Kingdom and the United States of America in order to obtain optimal seroconversion rates (Joint Committee on Vaccination and immunization, 1983; Advisory Committee on Immunization Practices, 1983).

The other vaccine-preventable diseases also have different epidemiological features in developing countries as compared with their characteristics in industrialized countries where the vaccines were originally developed. Since the epidemiology of these diseases determines the target groups, the epidemiological differences have important implications for decisions about who should be immunized and when. Such decisions will in turn affect the immunization schedules.

There are a number of developments currently taking place both with new vaccines and also with new immunization schedules - in terms of the age when the vaccines should first be administered and the periods between doses. The main goal of these developments is to fully immunize children as early during the first year, and with as few contacts with the health services as is possible for effective protection. Whilst such developments are likely to provide an important boost to the control of vaccine preventable diseases, it will be essential for them to be carefully monitored and evaluated before they are widely adopted. Two immunization schedules used in developing countries are outlined in Table VI (with that of the USA for comparison) which exemplify the variation in approaches to vaccine provision.

Table VI

Examples of two different Childhood Immunization Schedules for developing countries (excluding ante-natal tetanus) with that of the United States of America for comparison

1. Childhood Immunization Schedule: Recommendations of Expanded Programme on Immunization Global Advisory Group (EPI/GEN/85/1).

Age	Vaccines
Birth	TOPV[1], BCG
6 weeks	TOPV, DPT
10 weeks	TOPV, DPT
14 weeks	TOPV[2], DPT
9 months	Measles

1. TOPV = trivalent oral poliomyelitis vaccine
2. If the final dose of TOPV and DPT have not been given before 9 months of age they can be given simultaneously with measles vaccine.

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2. Childhood Immunization Schedule*: Kolda-Kaya-Kolokani Immunization Programme (Stoeckel, 1984).

Age	Vaccines
3-8 months	BCG 1st DPT & Polio (killed vaccine)
9-14 months	Measles, Yellow Fever 2nd DPT & Polio (killed vaccine)

* For mobile teams in the absence of fixed centres.

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3. Recommended schedule for active immunization of normal infants and children - United States of America (Advisory Committee on Immunization Practices, 1983).

Recommended age*	Vaccine(s)	Comments
2 months	DTP[1], OPV-1[2]	Can be given earlier in areas of high endemicity
4 months	DTP-2, OPV-2	6-wks, 2-mo, interval desired between OPV doses to avoid interference
6 months	DTP-3	An additional dose of OPV at this time is optional for use in areas with a high risk polio exposure
15 months	MMR[3]	
18 months	DTP-4, OPV-3	Completion of primary series
4-6 years	DTP-5, OPV-4	Preferably at or before school entry
14- 16 years	Tetanus toxoid	Repeat every 10 years throughout life

* These recommended ages should not be construed as absolute ie. 2 months can be 6-10 weeks etc.

1 DTP - Diptheria and tetanus toxoids and pertussis vaccine
2 OPV - Oral, attenuated poliovirus vaccine contains poliovirus types 1,2 and 3.
3 MMR - Live measles, mumps and rubella viruses in a combined vaccine.

Vaccines - storage and seroconversion

While it is relatively easy to change the "software" (the schedules) of vaccination programmes from developed countries to suit the requirements of developing countries (Halsey & Galazka, 1984), the "hardware" (the vaccines themselves) have sometimes proved to be much less adaptable. For example, it has already been noted that it is not generally possible to obtain satisfactory antibody production with currently available measles vaccines if they are administered to children less than nine months of age, because of the passively transferred maternal immunoglobulins (Black et al, 1984; Dick et al, 1975; Heymann et al 1983; Job et al, 1984). Since it would be epidemiologically desirable to immunize children against measles as early as six months (or even before), currently available vaccines are, in many ways, inappropriate to the needs of developing countries. If the vaccines had originally been developed with a younger age group in mind, might this problem have been overcome some years ago?

Not only are the epidemiological characteristics of the diseases different, but the response to the vaccines, in terms of antibody production, has sometimes not been so good under field conditions in developing countries. There are several reasons for these differences. The most important is that all vaccines, particularly those which consist of live organisms, have storage requirements which must be ensured if their potency is to be maintained. Temperature and light are the two major environmental factors which may decrease the ability of vaccines to stimulate an immune response, of which temperature is the most important.

In the past, live poliomyelitis and measles vaccines have been notoriously sensitive to temperatures above $4^{o}C$. While this continues to be a major problem for poliovaccines, recent developments in vaccine technology have produced measles vaccines which are much less heat labile. Nonetheless, many vaccines need to be kept cold from the time that they are manufactured to the time that they are administered (hence the "cold chain"). If these conditions are not maintained, the

viability of the vaccine is destroyed and it becomes ineffective. These rigorous temperature requirements have often been extremely difficult to achieve under field conditions in developing countries, with the result that a varying proportion of the vaccine which has been administered has been incapable of stimulating antibody production (Melnick, 1984; McBean et al, 1976; Anonymous, 1974; Carrasco et al, 1982).

These cold chain problems have been tackled on a number of fronts, from the development of more robust vaccines to the design of fridges and cold boxes which are more effective and easier to maintain under the difficult field conditions encountered in developing countries (Cheyne, 1982; EPI, 1984b; EPI, 1984c). Heat sensitive indicators have also been produced which provide health workers with information about whether or not the cold chain has been successfully accomplished - which in turn informs them of whether or not the vaccines are likely to be viable (EPI, 1984d). Training and supervision in the storage of vaccines and the maintenance of refrigeration equipment have also been greatly expanded. Despite these advances, however, problems will continue to arise if, as is so often the case, supplies of fuel, whether electricity or kerosene, are not dependable. The management and logistics of maintaining the cold chain are still a major challenge to national immunization programmes.

Other reasons why the response to vaccines has been less than satisfactory are: vaccines (notably measles vaccine) have been administered to infants younger than the recommended age, when transferred maternal antibodies interfere with their response to the vaccine; malnourished children are less able to produce antibodies to some vaccines than adequately nourished children and in some circumstances this has resulted in suboptimal seroconversion rates (although this fact should not be a contra-indication to immunizing malnourished children, who remain a priority group); and finally, for reasons only partially understood, oral polio vaccine has not proved to be as effective at inducing seroconversion in some communities in developing countries as it has been in developed countries (John & Jayabal, 1972; John, 1985).

Vaccines - administration and contra-indications

The efficacy of vaccines is not only dependent on satisfactory storage but also on ensuring that the defined target groups receive the vaccines and that the vaccines are properly administered. Once again, the need for adequate training and supervision are paramount, both to make certain that the vaccines are given in a way that ensures their effectiveness and also to guarantee that immunization does not give rise to unnecessary complications, such as abscesses or even hepatitis, as a result of inadequate sterilization of needles and syringes. If training, equipment and supervision are inadequate it is possible for vaccines to be potentially harmful as a result of contamination at the same time as they fail to be beneficial because of inadequate storage° Simple and effective sterilization techniques and appropriate syringes still require further development (Henderson R, 1984a).

In terms of the target groups for inclusion in the programme, these will be defined by the specific epidemiological characteristics of the disease. This information, and its rationale, clearly needs to be conveyed to the health workers responsible for immunization and, of course, to the community. The fact that the vaccine-preventable diseases in developing countries differ, epidemiologically, from their occurrence in developed countries has implications not only for decisions about target groups but also for decisions about contra-indications to immunization. As previously mentioned, such contra-indications are relative rather than absolute.

Since there is a small risk that concurrent mild febrile illnesses can occasionally give rise to complications following immunization this may be sufficient reason in developed countries to postpone the administration of measles vaccine, because the complications of the disease are relatively uncommon and it is easy for most mothers to return the following week to have their child immunized. In developing countries, however, mild febrile illness should not be a contra-indication to measles immunization. A relatively rare or minor

complication is an acceptable risk to take since the disease itself is severe, often fatal, and mothers' contacts with the health services (in particular their contact with the "immunization team") are usually difficult and infrequent. It is therefore unjustifiable not to include children in immunization sessions in developing countries with problems which would be adequate reasons to exclude them in developed countries (Galazka et al, 1984). This is a particularly important consideration for people providing curative services, since this is likely to be one of the rare contacts which young children make with the health services, and unless there is a major contraindication every opportunity should be taken to immunize them at this time - which unfortunately is often not the case (EPI, 1984m).

To a certain extent the focus of immunization programmes is not only the individual but also the community. This may be a difficult concept for health workers either to accept or to explain, since it is quite different to the emphasis of many other medical interventions. For example, it is widely accepted that a very small number of children who receive pertussis vaccine (fewer than 1 in 100,000) will suffer from serious neurological problems (Miller et al, 1981). This has, in the past, led to a debate in a number of industrialised countries about whether the benefits outweigh the risks of this vaccine (Editorial, 1981; Hinman, 1984b). However, unlike the situation in these industrialised countries, pertussis is a major cause of morbidity and mortality in developing countries (Mahieu et al, 1978) and the risk of serious complications following natural infection greatly outweighs the risk of complications related to the vaccine (Muller et al, 1984) - although this is likely to be of little comfort to the families of those few children who are adversely affected by the vaccine. With the advent of acellular pertussis vaccines it is likely that the balance in favour of immunization will become even more impressive. At a commmunity level, very young infants who are not protected by passively transferred maternal antibodies may be indirectly protected from pertussis before they are fully immunized if older children are successfully immunized. This should decrease the chances of younger children coming into contact in the home environment with the organism responsible for this diseases.

Finally, it is important for health workers and members of the community to understand that occasionally vaccines which are optimally stored and administered will not prevent the diseases, since none of the vaccines is 100% effective. Since the percentage of unavoidable vaccine failures will remain constant for each vaccine, the total number of vaccine failures will increase as the number of children who are vaccinated increases (EPI, 1979).

Information for planning, surveillance and evaluation

One final example of problems of technological transfer from developed to developing countries concerns the techniques which are available for obtaining the information which is essential for the effective planning, surveillance and evaluation of immunization programmes. Whilst the routine recording of health service activities, the notification of infectious diseases and the registration of cause-specific mortality data may all leave much to be desired in developed countries, they have attained a relatively sophisticated level when compared with the routinely available data which are available in most developing countries. Similarly, the opportunities for carrying out serological or other detailed epidemiological studies in developed countries are much greater than they are in developing countries.

The systems of surveillance and evaluation which have been used in developed countries to describe the problem and define high risk groups; to assess the effectiveness of immunization programmes; to examine their impact and to identify ways in which the vaccines have altered the epidemiological characteristics of these diseases, have often either been unavailable or incomplete in developing countries (Fine & Clarkson, 1982; Evans, 1984). The results of this have been that the full extent of the problem of these diseases has often not been appreciated and that the defects of existing immunization programmes have not been identified (EPI, 1982; Foster et al, 1984).

There have been a number of attempts to develop techniques of surveillance and evaluation which are more appropriate to the

conditions which exist in developing countries (Bernier, 1984b; Dondero, 1984; EPI, 1984a; EPI, 1984p; Heymann et al, 1983; Strassburg, 1984). These include the refinement of random cluster methods for assessing coverage (EPI, 1979c; Henderson & Sundaresan, 1982; Rothernberg et al, 1985) the use of case-control studies for assessing vaccine efficacy (Smith, 1982; Smith et al 1984) and the development of sentinel surveillance systems (EPI, 1985b).

Information for planning, surveillance and evaluation is essential if immunization services are to be efficient, effective and equitable (Carrasco et al, 1982; Guyer & Antangana, 1977). The wider adoption of these new approaches for the collection of relevant data should assist with the identification of current defects - which will be the first step towards their solution. Both EPI and UNICEF have made major contributions to the surveillance and evaluation of national immunization programmes through incidence and coverage surveys and comprehensive programme reviews (EPI, 1979c; EPI, 1984f; EPI, 1984g; EPI, 1984h; Orenstein, 1984). The dissemination of technical information concerning the vaccine-preventable diseases and their control has been a major activity of EPI and a number of other organizations (Center for Disease Control, 1984; EPI, 1985c; International Children's Centre, 1985).

PROBLEMS WITH THE PROVISION OF IMMUNIZATION SERVICES

One of the basic pre-requisites of a successful immunization programme is the need to ensure that an effective vaccine is administered to all of the target population. This has not always proved to be easy in developed countries, much less in developing countries.

The availability, manufacture and purchase of vaccines

The first consideration is the availability, in country, of sufficient quantities of vaccine. This will depend on an accurate estimation of the vaccine requirements (in terms of the target population and likely vaccine wastage) and on the ability of the country to purchase or manufacture enough vaccine to meet these requirements. The first of

these problems will depend on an understanding of the epidemiological characteristics of the vaccine-preventable diseases in each country (although clearly a number of generalizations are possible), on the availability of reliable basic demographic data and on an assessment of the achievements of existing immunization programmes in terms of coverage and impact.

The second problem, however, is much more complicated. For most developing countries it is unlikely that it will be cost effective for them to manufacture vaccines. The capital and recurrent costs are so high for vaccine production that very large quantities of vaccine need to be made before in-country production is economically justifiable. Nonetheless, 15 of the 23 developing countries with populations greater than 20 million are currently producing one or more of the EPI vaccines (Henderson, 1984b).

Most of the vaccines currently available are manufactured in developed countries. However, the number of companies involved with the production of vaccines for the six diseases under discussion is decreasing. This is the result of a number of factors which range from the purchasing and forecasting policies of intergovernmental organizations to the fact that there are new vaccine priorities in developed countries and some of the EPI vaccines may be considered to be "high-risk, low-profit business". The implications of this decrease for the future availability of these essential vaccines are not at present clear, although obviously it is an important issue which warrants close and careful monitoring, particularly since there appears to be little current excess capacity to meet any sudden increases in demand (Peretz, 1983; Peter, 1985).

The specific vaccine requirements of developing countries have not always been the priority concern of much vaccine research and manufacture, although there have been notable declines in the costs of many vaccines over the years. Recent advances in the process of producing inactivated polio vaccine, for example, have made the price of this vaccine much more competitive. However, the high technology needed to manufacture vaccines is always likely to make certain

aspects of the Alma Ata declaration sound a little hollow in relation to this specific PHC activity, notably the exhortation to develop programmes "at a cost the community and country can afford at every stage of their development." Despite the fact that the cost of purchasing the vaccines is only a relatively small percentage of the cost of immunizing a child (Hendrickse, 1975), it is likely to be a relatively large percentage of the Ministry of Health's foreign exchange requirements for immunization programmes.

Although developments in vaccine manufacture may decrease costs, most poor countries will have to rely to some extent on external financial assistance (Ward, 1984). Despite the major financial contributions which have been made by UNICEF, WHO and through bilateral agreements, national governments in developing countries continue to have to pay for about 80% of immunization programme costs (Henderson, 1984b). Revolving funds for vaccine purchase (Carrasco, 1983; WHO, 1984) and direct economic aid, both from intergovernmental organizations and also through bilateral assistance programmes will clearly continue to be essential if many countries are to overcome the basic costs and foreign currency implications of vaccine purchase. However, in conjunction with the need for economic assistance with the purchase of the vaccines, there is also the need for a commitment to international monitoring and quality control of the vaccines which are manufactured (Melnick, 1984; Vallancourt, 1984).

Once sufficient quantities of the various vaccines are available, the distribution of these vaccines to the target population will depend on an effective infrastructure. This again raises a number of issues for developing countries. First, it needs to be reiterated that the success of any immunization programme depends on many activities in both the health and other related sectors as well as on the development of the general infrastructure of the country. Thus, not only will the expansion of the health service facilitate the provision of vaccines but immunization programmes will also be greatly assisted by developments in sectors such as transport, communications and education - which have obvious implications for external support.

Secondly, a number of policy decisions need to be taken about the provision of immunization services which will depend to a large extent on overall health policies. Thus, if there is a commitment to develop health services within the framework of PHC then immunization services, as one of the PHC activities, will need to be expanded within this overall approach. The balance between the public and the private sector, between rural and urban health services and between curative and preventive activities will obviously affect the provision of vaccines.

Cost-benefit and cost-effective studies

Apart from overall health policies, the epidemiological characteristics of the diseases and the target groups for immunization, economic factors will also need to be taken into consideration (Creese, 1979; EPI, 1979c; Grab & Cvetanovic, 1971). Although there have been relatively few cost-benefit analyses carried out in developing countries which have focused specifically on immunization, those which are available concur with similar studies that have examined immunization in developed countries, coming out strongly in support of immunization (Barnum et al, 1980; Creese & Henderson, 1980; Creese et al 1982; Mills, 1983; Ponnighaus, 1980).

Whilst it is likely that the results of these studies are generalizable to a variety of different settings in developing countries (accepting, of course, that the costs are likely to increase disproportionately as the immunization coverage increases) there is a need to identify ways of minimizing costs (Cumper, 1984) and to carry out more analyses of the cost-effectiveness of different strategies (Martin, 1984; Creese, 1984; EPI, 1982). These are much less likely to have general relevance, since costs vary quite significantly from country to country and within countries they may also vary depending upon the region and the target group (Cutting, 1980; Ponnighaus, 1980; Robertson et al, 1984). Costs are affected by a wide range of factors including the prices of inputs, the wages of health personnel, the development of the health infrastructure and the provision and utilization of health services, population density and access,the

target groups and the vaccines which are included in the programme.

The average national costs of fully immunizing a child vary from US$5-15. As an overall per capita cost to the health services this is equivalent to US$0.2-0.6, assuming that infants constitute about 4% of the total population (Henderson R, 1984b). However, even costs of this magnitude may be a serious problem for most of the poorest developing countries.

Since a large proportion of the costs of any immunization programme are fixed, increasing the numbers of children immunized and the number of vaccines included in the programme will decrease the average cost per immunization (although this balance is likely to change when special efforts need to be made to reach inaccessible groups or communities). This clearly poses a policy dilemma, because the most effective way to decrease fixed costs and increase coverage may be by means of vertical programmes. In fact, there is some evidence from Brazil that mass campaigns or intensified outreach programmes may be more cost-effective than routine on-demand services (Creese, 1984), although as has been pointed out, such analyses are not without their problems (Mills, 1985).

Vaccine distribution

There are basically three strategies for providing immunization services and the relative advantages and disadvantages of these are summarized in Table VII. In developed countries, immunization programmes have been predominantly based on static health facilities. In developing countries, where it is usually much more difficult for people to attend static services (for a variety of physical, geographical, infrastructural, cultural and motivational reasons), it is likely that improved coverage will depend on making more effort to take the services to the people. Outreach programmes are most likely to be able to improve the accessibility of the services whilst at the same time developing immunization services within the overall framework of PHC.

Table VII

Types of immunization service: advantages and disadvantages

STATIC (eg clinics and other health facilities)	**OUTREACH** (eg satellite services & mobile PHC teams)	**MASS CAMPAIGNS** (eg single vaccine total coverage; all vaccines offered according to need)
ADVANTAGES		
Other PHC services and health records are readily available.	Takes the services to the people (therefore relies less on people's motivation).	High coverage possible provided there is good planning and promotion, national commitment, intersectoral cooperation & community participation.
Easier to link immunization & other PHC activities - for staff & community.	Some other PHC activities could be provided at the same time.	High quality immunization service possible with adequate training.
Unnecessary for staff to travel (which decreases costs & inconvenience to staff).	Helps health workers to get to know their communities.	In some circumstances costs may be cheaper than alternative approaches.
Supervision & in-service training are easier.		Useful short-term measure (whilst the PHC infrastructure is being developed).
		Advantages likely to be greatest in areas of lowest coverage: useful for very dispersed populations.
DISADVANTAGES		
Success depends on the community's willingness & ability to use the service (eg transport, clinic hours).	Necessitates travel & per diem costs for staff.	Discontinuation or disruption of other PHC & health-related activities (during the planning and implementation phases).
Attendance likely to be affected, both positively & negatively, by the quality of the other services which are provided from these health facilities.	Increased inconvenience for staff.	Must be continued every year until the infrastructure can cope with routine immunization on demand.
Difficult to obtain good coverage until there have been significant infrastructural developments.	Supervision more difficult.	It may be difficult to maintain the enthusiasm which is necessary for the success of mass programmes.
Costs may be high if the population density is low.	Equipment & records less likely to be available.	Requires major intersectoral cooperation (eg schools, transport, media etc).
	May be vaccine wastage.	Difficult to link with other PHC activities
	Small numbers of people are contacted only.	
	The cold chain is more difficult to maintain.	

(See De Quadros, 1984; World Federation of Public Health Associations, 1984)

Although mass campaigns may achieve high coverage rates they are, of necessity, based on a vertical rather than an integrated approach to health care delivery. Certainly they can achieve impressive results, although whether these can be sustained remains to be seen (Asaad & Ljungarg-Esteves, 1984). In the Gambia, for example, measles was eradicated during the late 1960s through a mass campaign which achieved nearly 100% coverage.It returned as an endemic disease a few years later because it was not possible to maintain the mobile teams or the supplies of vaccine, nor was the health infrastructure sufficiently developed to cope with the identification and immunization of new susceptibles (Williams & Hull, 1983). A similar scenario occurred in Mozambique (Walt & Wield, 1983).

Mass campaigns frequently rely heavily on the participation of volunteers (National Coordinating Committee, 1984) whose support may be difficult to maintain as peoples' priorities and interests change. The involvement of volunteers can decrease the costs of providing vaccines and these costs may be further decreased if jet-injectors are used, which may be a particularly cost-effective and practicable option during mass immunization campaigns.. However, during such campaigns it will also be necessary to have more stocks of vaccine than are actually required, because of the difficulties of relocating vaccine supplies at short notice and the unpredictability of the demand for immunization (Risi, 1984).

If linked to basic infrastructural health care developments mass campaigns may be an appropriate short term measure for decreasing mortality and morbidity. However, they would seem to be an inappropriate long-term measure in countries which have adopted PHC policies. There is also very little known about the disruptive effects of such programmes on other health services or about the opportunity costs, both financial and otherwise, which may result from the diversion of resources from other routine activities (Ward, 1984). It has been stated (Risi, 1984) that mass campaigns (in Brazil) are justified because "the best immunization strategy...is that which most readily achieves the ultimate objective" (i.e. the control of vaccine preventable diseases). This would probably not be true in many

countries if the effective strategies which were adopted undermined or prevented the development of PHC services. The vaccine-preventable diseases are, in general, not of sufficient importance to warrant such allocation of resources.

None of the strategies outlined in Table VII are as clear cut as they might appear and there are many variations on these basic themes. For example, mass campaigns may include one vaccine or the full range of vaccines (Risi, 1984; National Coordinating Committee, 1984), they may provide total coverage for the target group or may merely be directed to susceptible children, and they may be provided in combination with routine services or as "catch-up" or "pulse" programmes (John et al, 1983; John et al, 1984). An additional decision which needs to be taken for certain outreach strategies and for mass campaigns in general is whether people should be immunized on a home-to-home basis or whether they should come to centralized collecting points. This decision will be affected by a number of factors including the cultural characteristics of the communities, population density and cost. For static health facilities decisions will need to be taken about whether immunization will be available routinely on demand or whether it will only be available on certain days.

Immunization and primary health care

EPI has recommended that immunization programmes should be developed as part of the PHC services. This will ensure that the management and logistics expertise which is so urgently required for the expansion of immunization services can be shared with other PHC services and vice versa (Bhargava & Sokhey, 1984; Henderson, 1984; Reid & Smith, 1984; Robinson, 1984; Vaughan et al, 1984). It should also help to prevent a situation arising in which children are protected, at great cost, from the vaccine preventable diseases only for them to die of other diseases which are also eminently preventable through effective PHC services (Kasongo Project Team, 1981). In addition, the provision of PHC activities as a "package" should encourage the use of a number of services when people visit the health centres. In the Gambia, for example, where high vaccine coverage rates have been achieved, 75% of

measles immunizations were administered to children attending for curative services. Coordination between immunization and curative services could also help to lower the fixed costs, which are a major component of the overall cost of immunization programmes, and could decrease the extent of the cold-chain requirements.

In the same way that decisions about strategies will depend on other policy decisions in the health sector and on a number of epidemiological and economic considerations,choices about who actually administers the vaccines will depend on the choice of strategy. If a mass campaign approach is adopted then it is unrealistic to expect the PHC workers to carry out all the immunizations. If immunization services are provided from static facilities, however, then there are obvious advantages to PHC workers being responsible for immunization as well as for the other PHC activities (Walker, 1982). This will depend, however, on their ability to take on an additional work-load. It will also depend on whether the extra training, supervision and logistic support can be justified by the potential number of people who might be immunized. A wide range of people have been effectively trained and supervised to adequately administer vaccines, from traditional birth attendants to teachers (World Federation of Public Health Associations, 1984). While some vaccines are obviously easier to store and administer than others, with sufficient training, support and supervision it should be possible for any vaccine to be administered by people with relatively little formal education - although it is very important, for surveillance and evaluation, that they should be able to maintain adequate records.

From this discussion about some of the decisions which will need to be taken about the provision of vaccines it will be appreciated that they are all interdependent. It needs to be emphasized, however, that these are not mutually exclusive decisions. Any combination of strategies which improves peoples' access to immunization services should be considered, taking into account the inter-related economic,epidemiological and organizational factors. As with all the other components of PHC there is clearly enormous scope for new and imaginative programmes (Harpham et al, 1985) - provided that these

develop from well evaluated pilot projects (Haxton, 1984; Reid & Smith, 1984).

At the same time, the vaccines not only need to reach the people but they must also be effective. This will depend on maintaining the cold chain and ensuring that the vaccines are properly administered. It will also depend on regular and appropriate methods of monitoring and evaluating the organizational strategies which are adopted. Such considerations provide support for those people who have asserted that the priority developments which are needed to improve immunization programmes are not simply technical but are also political, economic and managerial (Foster et al, 1984; Henderson R, 1984c; Henderson R, 1983): "The continuing death and disability from vaccine-preventable diseases in the developing world results from two fundamental causes - lack of sufficient political will to furnish the financial and human resources required and lack of management skills to translate resources into results" (Henderson, 1984). Nonetheless, it needs to be appreciated that the control of vaccine preventable diseases is only one health issue among many which will require international and national "political will" if effective solutions are to be realized.

PROBLEMS WITH THE UTILIZATION OF IMMUNIZATION SERVICES

For immunization programmes to have a major impact on vaccine -preventable disease they not only need to ensure that effective vaccines are accessible to the target population but they also need to make certain that the services which are provided are used. Provision and demand need to be developed in parallel: there is little point in increasing one without the other. In many developing countries utilization is poor, both because people do not attend for initial immunization and also because a large percentage of those who do attend fail to comply with the repeat visits which are necessary for all vaccines, with the exception of measles and BCG (Martin, 1984; Henderson, 1984). It is not uncommon for drop-out rates between the first and third visits to exceed 50%, which means of course that the initial coverage in many countries is much higher than the rates provided in Table III.

Legislation and education

In developed countries, legislation has been used to good effect in improving utilization. However, it is unlikely that this will play a major role in many developing countries, although the possibilities are obviously worth exploring. For example, evidence of completed immunization as a criterion for school entry is unlikely to be very effective if the most at-risk groups do not attend school and if the most important time for children to be immunized is during the first year of life.

Helping the community appreciate the need for immunization and making people aware of the services which are available are clearly necessary if not sufficient activities for increasing utilization. There also continues to be a need for "advocacy", to provide influential people with information about the vaccine-preventable diseases and their importance and about what needs to be done to control them. For immunization programmes to be successful they will require political support and the allocation of sufficient resources.

In addition, information will also need to be provided to communities in order to generate discussion and create or support a demand for immunization (Guyer & Antangana, 1977; Jinadu, 1983). This should include general information about vaccine-preventable diseases, the reasons why vaccines are important, the target groups for immunization and the side-effects of the vaccines (Alakija & Anakhu, 1983; Dhillon, 1983). Whenever possible, health education about the vaccine preventable diseases should be linked to related health problems, such as diarrhoeal diseases and malnutrition, and to other PHC activities which have an impact on these diseases, for example maternal and child health services (including the advantages of child spacing), curative services and nutrition. Furthermore, it is essential for parents to know, specifically,what immunization services are available, where and when, and who should attend for immunization, at what age and how often. There is generally a need to develop innovative and more effective approaches to educating and communicating with communities (Walt & Constantinides, 1984).

Community participation

It is likely that people's acceptance and use of immunization services will be influenced by whether these services are consistent and reliable, by their attitudes to other PHC services and by their relationships with the PHC workers. However, utilization of the services will also depend on whether the consumers' needs have been taken into account when decisions have been made about where, when and how vaccines are provided. This requires health workers not only to have an understanding of the most convenient times and places for providing immunization services but also to have developed general skills in promoting community participation (MacCormack, 1983). It further necessitates the identification of obstacles to utilization and the reasons why people either do not attend or do not complete their schedules. This in turn will require systems of surveillance and specific surveys (Akesode, 1982; Belcher et al, 1978; EPI, 1977; EPI, 1984h; EPI, 1984n; Markland & Durand, 1976; Odebiyi & Ekong, 1982; Rahman et al, 1982). When such surveys have been carried out they have identified a variety of problems, from lack of knowledge about the vaccine-preventable diseases and lack of confidence in the vaccines to the negative effects of seasonal or urban migration on attendance.

In terms of community involvement there are obviously a number of issues with which communities will not be involved. Decisions about which vaccines to include in the programme, the schedules and the strategies are usually based primarily on epidemiological and economic considerations. However, with recent vaccine developments there is increasing flexibility, with a move towards completing immunization as early as possible. The exception to this is measles vaccine which , with currently available vaccines, should not be administered before 9 months of age - an awkward age for mothers, since children are still too young to walk and are becoming heavy to carry. However, developments with measles vaccine give some cause for optimism about the possibility of a vaccine becoming available which could be

administered earlier than nine months (which would also be epidemiologically preferable). There have also been developments with DPT and inactivated polio vaccines (IPV) with the intention of decreasing the number of doses which are required (Mahieu et al, 1978; Salk, 1984; Van Wezel et al, 1984). However these developments remain at a relatively early stage of their research and require more extensive substantiation before they can be considered for general adoption.

Recent developments

There have been a variety of encouraging developments in a number of countries which have had a major impact on vaccine coverage. Although the specific activities differ depending on the conditions and the immunization policies of the countries concerned, there are a number of general principles which are evident in all of the more successful programmes (EPI. 1985a; Haxton, 1984;National Coordinating Committee, 1984; Reid & Smith, 1984;Risi, 1984; Task Force for Child Survival, 1985; UNICEF, 1985; World Federation of Public Health Associations, 1984):

* Evaluation of existing programmes: it is essential to have an understanding of why parents do or do not take their children for immunization. What factors affect utilization, how accessible are the services and what are the existing obstacles to achieving immunization-for-all? Programme reviews and special surveys indicated a number of reasons, including: socio-cultural factors affecting beliefs and customs which adversely influence utilization; lack of knowledge about, or even negative attitudes towards, immunization; inconvenient geographical access and opening times of immunization sessions; conflicting commitments and insufficient time or money to attend for immunization; and a large number of logistic and managerial factors which affect the availability of vaccine supplies and the quality of the service which is provided. The identification of such problems will be the first step towards overcoming or avoiding them.

* Involvement of the community: the need to involve the community at the beginning of new immunization initiatives, rather than as a fashionable afterthought, is being increasingly appreciated. What is also being recognized is that resources, not simply good will, are essential to motivate people to become involved and to maintain their interest and commitment. Members of the community can participate in a variety of activities including assisting with the initial surveys to assess coverage, to estimate the incidence and prevalence of the vaccine preventable diseases and their associated disabilities, and to identify the problems with existing programmes; planning and implementing new initiatives (both getting the vaccines to the people and also getting the people to the vaccines); and monitoring and evaluating the progress of immunization programmes.

* Political commitment: this has proven to be necessary at both central and local levels and is essential for several reasons, from encouraging people to attend for immunization to counteracting rumours and misinformation. The enthusiasm and support of politicians, cultural and religious leaders and other individuals who influence peoples' ideas and decisions are clearly important for the success of a programme. Methods of advocacy need to be identified which will not only generate but also maintain the interest and commitment of politicians and community leaders in view of the long-term nature of immunization programmes.

* Multisectoral cooperation: there are two aspects of multisectoral involvement and coordination which need to be considered. First, a number of different government departments will need to participate in immunization programmes, including education, social services, community development, transport, and, of course, planning and finance. For example, the Ministry of Education will be important because school children constitute a unique opportunity to carry the messages of immunization into peoples' homes and because schools may provide suitable sites for giving the vaccines in outreach programmes or mass campaigns. Secondly, the media, the private sector, non-governmental organizations, cultural, religious and other

community groups and even the armed forces and the police have shown that they can have important roles in immunization programmes.

* Adequate planning, management, training and supervision: a number of related factors have been shown to be important for increasing the coverage of immunization programmes. These include clearly defined and realistically achievable objectives; a management system capable of ordering, storing and distributing the vaccine supplies; appropriate sites and suitable times which are convenient for people to attend for immunization; mechanisms for handling non-attenders, drop-outs and the occasional adverse side-effects of immunization; and data collection systems for surveillance and evaluation which ensure that health workers appreciate the need for such information and that the collated and analysed statistics are fed back to the people responsible for their collection. All of these issues require an effective planning and management system and there are obvious advantages to first trying out new approaches as pilot projects before they are more widely adopted. It is axiomatic that adequate training and supervision are fundamental to immunization programmes, and during programme reviews the inadequacies of such activities have often been identified as major obstacles to the achievement of high coverage rates. One of the main activities with which the EPI has been involved is the development of training programmes which are adaptable to the specific requirements of different countries. Such training programmes focus on both the technical and also the management issues of immunization programmes, are directed to people at many different levels within the health infrastructure, and, whenever possible, link immunization to other PHC activities.

* Information dissemination: techniques for disseminating the why, who, where, when and how often messages have also been of paramount importance to immunization programmes. A number of different approaches have been tried which include: the use of the mass media (press, radio and television) and the involvement of media personalities and celebrities; the design of symbols or mascots with which people can easily identify and which they come to associate with

the immunization programme; leaflets, car stickers and mobile megaphones; music, drama and other attention drawing activities (for example, firework diplays); and the use of school children, extension workers and health staff both to take the messages into peoples' homes and also to discuss them on a one-to-one basis. There are many opportunities to try new approaches, the best of which will build on cultural beliefs and use traditional methods, both formal and informal, of spreading information in the community - systems which have sometimes demonstrated their great potential by spreading negative messages about immunization programmes, rapidly and effectively°

7 POLICY IMPLICATIONS AND CONCLUSIONS

Controlling the vaccine-preventable diseases should be an extremely attractive option to national governments and international organizations involved with health care in developing countries. These diseases are, for the most part, major causes of morbidity and mortality, and the technology is available to have a significant impact on their incidence - technology which has generally been shown to be effective in a variety of different situations. There is increasing evidence of some impressive progress in the control of the vaccine-preventable diseases through the coordinated activities of intergovernmental organizations; bilateral assistance programmes; non-governmental organizations; and host governments themselves (who have ultimately carried the major burden and responsibility for these achievements).

However, despite these developments, there is still a long way to go. It would be unrealistic to expect too much too quickly in view of the many factors which have a bearing on the incidence of these diseases and which also have a negative impact on control programmes. Transforming potential prevention into effective control is always difficult and will require clear choices to be made from a number of policy options. In terms of immunization it is going to be a major challenge to make contact with all pregnant women at least twice in their pregnancy, all newborn babies and all infants at least three times, at predetermined intervals and places, by the age of nine months°

Table VIII provides an indication of some of the planning questions which need to be answered, at all levels within the health system.

Table VIII: Some policy & planning questions about immunization programmes & possible associated actions (Adapted from Dick,B., 1985)

Questions to be asked			Possible actions
Are vaccine-preventable diseases a priority health problem?	No	Is sufficient information available to make this statement? Is this the result of a successful immunization programme?	Information collection Research Continued support
Yes			
Have groups at high risk from vaccine-preventable diseases been identified?	No	Insufficient information available from routine sources Lack of expertise/interest/concern/resources to obtain information	Information collection Research Advocacy Training & Allocation of resources
Yes			
Is there a national policy on immunization and is this compatable with the overall health policy?	No	National decision makers unaware/unconcerned about vaccine-preventable diseases Ministry of health underdeveloped, uncommitted to PHC or in conflict with donor policies	Information dissemination Advocacy & support
Yes			
Who is participating in the planning, implementation, surveillance and evaluation of the immunization programme?		Ministry of health and other health-related ministries Intergovernmental organizations (eg EPI, UNICEF) Non-governmental organisations (national and international) The private sector, industry and commerce, the media The "people" - community leaders, community groups, political, cultural and religious organisations, etc	These factors will affect the type of activities which are required/possible
How and by whom are the vaccines being distributed and administered?		Outreach programmes - mobile teams/house-to-house visits Static health facilities - clinics and PHC centres Mass campaigns	
Is the vaccine coverage suboptimal? (ie. less than 90%)	No	Effective immunization programme Sufficient information not available to be confident about this statement	Continued support Information collection
Yes			
Have the current immunization activities been reviewed/evaluated	No	Insufficient expertise/resources/interest	Assistance with techniques and resources
Are there technical problems or problems with provision?	Yes	Inadequate health infrastructure/lack of concern or enthusiasm Insufficient resources (money, equipment, supplies or people) Lack of skills (management, maintenance) Insufficient community involvement	Advocacy Community participation Training Assistance with resources/service provision. Technological developments
Are there problems with utilization?	Yes	Inappropriate provision Poor community participation Lack of knowledge about vaccine-preventable diseases and vaccines Lack of knowledge about the immunization programme	Health education Community Participation Assistance with provision

Immunization and general health policy

The discussion of any specific PHC activity, such as immunization, raises a number of general issues which apply to all components of health programmes: how to generate the political will to do what needs to be done; how to put policy into practice; how to define priorities; and how to cope with the conflicting demands not only within the health sector but also between health and other sectors, such as defence or education?

The control of vaccine-preventable diseases depends on a number of different PHC activities which affect their prevention, diagnosis, treatment and rehabilitation. Furthermore, their control will both affect, and will also be affected by programmes directed at other causes of childhood morbidity and mortality (for example, diarrhoeal diseases), and by other PHC activities, such as nutrition and family spacing programmes. Whilst immunization programmes should have their own objectives, these need to be seen within the context of the overall objectives of the health services (is the goal lower infant mortality or decreased mortality from vaccine-preventable diseases?). Immunization is not an end in itself and it is important that immunization services should avoid becoming monopolistic, but should remain a part of the overall development of PHC.

Many of the PHC ideals will take a very long time to be realized. There may be advantages, both for peoples' health and for the morale of health workers, to make some relatively rapid progress with interventions such as immunization. Such vertical programmes may be justified if they can strengthen the PHC services at the same time as achieving quick results. However, it will be necessary for governments to ensure that in the process of achieving these short-term successes they do not syphon off the resources which are needed for basic PHC developments. Problems may also arise in the future if people's enthusiasm cannot be maintained or if health personnel involved with a high visibility, politically powerful and effectively functioning vertical programme are not willing to risk a decrease in the quality or

quantity of their service by moving from a vertical to a horizontal programme - even if this were only to be partially integrated,at the "sharp end".

In addition to the on-going debates about vertical and integrated programmes, a number of other general health sector problems will affect immunization programmes: how to generate and sustain "community participation"; how to develop the necessary management skills at district level; how to work with the private sector and with donor agencies whose priorities and interests may not be the same as those of the Ministry of Health? What is clear is that there are unlikely to be any simple, universal solutions to these problems which will be "right" for all PHC activities or for all situations.

It is obvious that the formulation of health policies in general and the degree to which these have moved along the path from words to action will have a major influence on immunization programmes and on other aspects of the control of vaccine-preventable diseases. The development of the health and health related services are major factors which will determine whether it is possible, using existing staff and facilities, to provide vaccines regularly and systematically. The extent to which health services are decentralized will also affect the way immunization services are delivered. Similarly, general decisions about training (how it is done, how often it is reinforced and how much support and supervision is given to the people once they are trained) will also specifically affect the provision of vaccines.

The issues extend further than the activities of the Ministry of Health. They include the degree to which the private sector and non-governmental agencies are operationally involved with the provision of health care, and the control which the Ministry is able to exert over them - either in the form of a carrot or a stick. Additionally, attitudes towards traditional healers, particularly traditional birth attendants, and their involvement with the statutory health services, will be likely to affect the provision and, perhaps more importantly, the utilization of immunization services.

Immunization programmes and donor agencies

Since the early 1970s there has been increasing interest in immunization from WHO and UNICEF, non-governmental organizations (for example the Save the Children Fund's "Stop Polio" campaign, Rotary International and a number of Red Cross and Red Crescent Societies), bilateral assistance programmes and groups such as the Task Force for Child Survival.

Whilst international interest and involvement are important, they may also introduce new problems. There appears to be an increasing trend among some donor agencies to favour short-term vertical programmes which have rapid, measurable results and which do not have long-term revenue implications for the agency. In addition, these programmes often emphasize the technical aspects of health care provision. Whilst this trend is understandable, since accountability and effectiveness are clear, such a focus may adversely affect the longer term developments with outcomes which are less easily quantifiable.

Although donors often have short-term horizons and lean towards these vertical programmes, Ministries of Health may be much more concerned about the sustained development of health services, with immunization as only one part of a PHC package (although clearly many Ministries of Health also see advantages in achieving rapid high visibility results). In such a situation, donors may be asked to provide logistic support (refrigerators, vehicles, vaccines) and training (manuals and workshops) to help the Ministry of Health build up local services. Donors then have less control over their inputs, and the use which is made of them, than if they support a vertical programme which has its own office in the Ministry of Health and its own personnel working from mobile clinics.

The possibility of conflict between the policies and aspirations of Ministries of Health and those of donor agencies may also be reflected at field level. For example, donors may insist on Ministries of Health providing more resources (of personnel for instance) than they

would ordinarily wish to direct into immunization activities. Such an approach could divert a disproportionately large percentage of the national health service resources and the interest and activities of the staff. There is a need for a much better analysis and understanding of the effect of such donor involvement with immunization on other PHC activities, not only in the obvious case of mass campaigns, but also more generally.

Providing immunization services

How vaccines are provided, as has already been noted, depends on a variety of factors including national health policies, the influence of donor agencies, the development of health and related services and the population size and density. Since several of these factors will vary considerably within, let alone between, most developing countries, approaches to vaccine provision will need to be flexible. There is scope for experimenting with different systems and with the involvement of different people for actually giving the vaccines.

There is little doubt that mass campaigns are able to achieve rapid increases in coverage and similarly impressive decreases in disease incidence - high visibility inputs and outcomes (although high visibility carries it own dangers, particularly if programmes are not successful or sustainable). In addition, mass campaigns are able to harness the energy and enthusiasm of many groups, particularly volunteers, who would probably not be willing (or even able) to be involved on a more regular basis.

However, a number of questions remain to be answered about mass campaigns: what is their effect on other programmes and PHC activities? Is it going to be possible to sustain the momentum and keep peoples' interest and enthusiasm? If not, this may, in the long-term, have a negative effect on attitudes to immunization and even on the diseases themselves. How replicable are the achievments of mass campaigns - if they work in Central and South America are they necessarily going to be an appropriate solution for countries in Africa?

Ways of making the best use of available resources need to be identified. For example, it may be possible to make a case for targeting immunization services to high risk groups - although, while this may optimize the financial costs, the costs in political terms may be high, since it is often difficult to raise resources for the powerless constituencies who are usually particularly vulnerable.

The difficulties of controlling the vaccine-preventable diseases emphasize the need to grapple with the conflict between what is ideal and what is possible. For example, the overall health policy may be to provide all PHC services from static clinics, so that families can receive a variety of preventive and therapeutic services at the same time (the "supermarket" approach). However, the population covered by these static facilities may not be sufficient to justify the equipment, training, logistic support or supervision necessary to provide adequate immunization services on this basis. Outreach programmes and the use of "immunization teams" may therefore be the only practical solution in some areas - although their success, in turn, will depend on adequate community organization and on a number of factors which may vary a great deal even within a particular country (for example seasonal accessibility and the reliability and availability of transport and supplies of vaccine).

Resources and costs

As a result of the increasing international commitment to immunization, it is likely that external resources will be available to support and expand national immunization programmes. The requirements for such assistance will depend on the overall development of the country and of the health services, and on the current status of immunization programmes. It will also be affected by whether or not the country in question is manufacturing any of the vaccines required for routine immunization.

Once again, such support has repercussions. If resources are provided for immunization, this may mean that support will not be available for other PHC activities which have an impact on infant and childhood mor-

bidity and mortality. It may even attract resources away from other PHC activities which will almost certainly negatively affect their quantity and quality.

External resources also tend to have considerable recurrent cost implications. Who is to be responsible for such long-term resource requirements? Ministries of Health may be quite unable to support expanded immunization programmes with existing available funds. Vaccine costs are also likely to vary, and any fluctuations will have serious repercussions on immunization or, if immunization programmes are to continue unaffected, a knock-on effect on other PHC activities. Most of these external resources will ultimately come from the national governments of industrialized countries. Although for them the vaccine-preventable diseases are generally not the kind of priority that smallpox was during the smallpox eradication campaign, as regional eradication programmes for measles and poliomyelitis are accomplished it is likely that the concern and commitment will increase.

The cost benefits of preventive programmes for the vaccine-preventable diseases are no longer in question. What needs much further work, however, is the identification of the most cost-effective ways of providing these vaccines to different groups and to people living in different regions of developing countries.

Surveillance and evaluation

If the available resources are to be optimally utilized in immunization programmes it is going to be very important to ensure that each programme has adequate systems for surveillance and evaluation. This will be achieved through routinely collected statistics, possibly from sentinel facilities, supplemented by ad hoc surveys (which, using recently refined techniques, will be able to explore in more detail a number of issues, from vaccine coverage to the reasons why coverage is suboptimal - both in terms of the provision and the utilization of services).

As with other aspects of PHC it will be important to appreciate that the collection of reliable and relevant statistics will require resources, and these should be specified when programmes are designed. Furthermore, the people responsible for collecting routine statistics will need to receive adequate training, supervision and feedback if the quality of the data which they collect is to be maintained.

Adequate surveillance and evaluation will not only be important for Ministries of Health but will also be essential for donors. With the increasing demands being made on potential sources of external support, donors are becoming more and more concerned about the effectiveness of their assistance. In this regard immunization programmes are more fortunate than many other aspects of PHC, because techniques for measuring coverage and disease incidence are now well developed and are relatively easy to carry out in the field.

The future

There continues to be a need for technical developments, including more potent, less reactive vaccines, which can be given earlier in life and which require fewer doses, and improved equipment for the storage and distribution of vaccines (for example cold chain and sterilizing equipment). There is also a need to develop new approaches to providing the vaccines and improving utilization.

Concerning the technical research, it is likely that much of this will continue to be carried out in countries where, in general, the main research efforts and funds are being directed to more "fashionable", and for them more priority diseases. It will be important that the six vaccines which are the focus of EPI remain on the research and development agendas of international funding and manufacturing organizations. This will be a major challenge and is linked to many factors such as "North-South" relations and international health policies. It will also be important to ensure that advances move successfully from the laboratories and pilot projects into national immunization programmes and that they have a measurable impact on the

incidence of the vaccine preventable diseases. Such considerations will also be necessary if vaccines are successfully developed for priority diseases other than the current EPI target diseases. These are likely to raise a number of questions concerning their possible inclusion in national immunization programmes.

However, many of the research requirements are of an applied nature. Encouragement and support needs to be given to implementing these as part of management and the process of planning: defining the problem (incidence and coverage surveys), identifying solutions (why people are not attending for immunization and the characterization of obstacles to provision and utilization), surveillance and evaluation (including the monitoring of the vaccines, of their long-term protection, and of possible changes in the epidemiology of some of the vaccine preventable-diseases with rising socio-economic conditions and increasing but sometimes patchy coverage). There is a need to develop and assess new approaches, to improve health education and community participation and to experiment with ways of organizing the services (what are the implications of current approaches for women's time, especially poor rural women; why do people not attend for immunization even though they know about its importance; why are the drop-out rates often so high?) Immunization programmes still have much to learn from the analytical techniques of operational research and the behavioural sciences.

A long-term perspective on immunization programmes will be essential because the continued provision of vaccines will be necessary for many years to come. It is also important because it emphasizes the need to think about recurrent costs; about the possibility of fluctuations in external support; and about ways of maintaining the enthusiasm and commitment of the international community and of national politicians, health workers and communities.

Whilst many of the problems of the control of vaccine-preventable diseases are universal, it is usually not possible to generalize about solutions, except in the broadest manner. However, given that the technology is available to control these diseases (and that this tech-

nology is constantly improving), and that the political will to do what needs to be done is increasing, the future looks promising for the strengthening and expansion of national immunization programmes in developing countries. These should make a major contribution to the quality of life of all communities in developing countries, both directly by their effect on the vaccine-preventable diseases and also indirectly by their positive impact on primary health care.

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